II. REMARKS

Formal Matters

Claims 1, 4-8, and 11 are pending after entry of the amendments set forth herein.

Claims 1, 4-8, and 11 were examined and were rejected. Claims 12-35 were withdrawn from consideration.

Claims 1 and 5 are amended. The amendments to the claims are made to place the application either in condition for allowance or in better form for appeal and thus are solely in the interest of expediting prosecution, and are not to be construed as acquiescence to any objection or rejection of any claim. Support for the amendments to claims 1 and 5 can be found in the claims as originally filed, and throughout the specification, in particular at the following exemplary locations: page 14, line 11 to page 15, line 5 and page 16, lines 8-9. Accordingly, no new matter is added by these amendments.

Applicants respectfully request reconsideration of the application in view of the remarks made herein.

Rejection under 35 U.S.C.§112, first paragraph

Claims 1, 4-8, and 11 were rejected under 35 U.S.C.§112, first paragraph, as allegedly lacking written description.

The Office Action states that the specification fails to set forth a disclosure of a specific agent suitable for use in practicing the claimed invention. The Office Action concludes that a catalog of potentially effective agents is deemed an insufficient written description of an agent of the claims because it would not reasonably convey to a skilled artisan that the Applicants had possession of the claimed invention at the time the application was filed.

Applicants respectfully traverse the rejection. According to the MPEP §2163.02 all that is necessary to fulfill the written description requirement is that Applicants convey to a person of ordinary skill in the relevant art that Applicants were in possession of the claimed subject matter. In other words, to satisfy the written description requirement, Applicants need only show that one of skill in the art would recognize that the Applicants invented what is claimed. Possession may be shown in a variety of ways, including by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention.

The present invention is based on the novel discovery that overexpression and accumulation of apoE causes hypertriglyceridemia by stimulating VLDL production and by impairing VLDL lipolysis. It necessarily follows that reducing the plasma level of active apoE will also reduce the plasma level of

VLDL. Those skilled in the art are well aware of variety of agents that reduce expression of a coding region (e.g., apoE), including agents that affect promoter activity, antisense nucleic acids, and ribozymes. Accordingly, there is no need to list each and every such agent to show that Applicants had possession of the invention at the time of filing. However, to expedite prosecution and advance the claims to issuance, claims 1 and 5 are amended to cite specific classes of agents that may be used in accordance with the claimed methods. Specifically, claims 1 and 5 are amended to recite that the agent is selected from the group consisting of: antisense nucleic acids, ribozymes, and antisense conjugates.

The sequences of apoE mRNAs were known as of the April 12, 1999 priority date of the instant application and available to the public. See, e.g., GenBank Accession No. M12529 – apoE mRNA sequence, published August 8, 1995; Breslow et al. (1982) *J. Biol. Chem.* 257:14639-14641 – human apoE cDNA sequence; and McLean et al. (1984) *J. Biol. Chem.* 259:6498-6504 – human apoE3 cDNA sequence.

Additionally, several texts were published as of April 12, 1999 that provided detailed descriptions of how to make and use antisense nucleic acids. See, e.g., "Antisense and Ribozyme Methodology: Laboratory Companion" I. Gibson, ed., Chapman & Hall (1997); and "Applied Antisense Oligonucleotide Technology" C.A. Stein and A.M. Krieg, eds., Wiley-Liss (1998). These texts are evidence for the fact that those skilled in the art as of the priority date knew that all one needs to make antisense nucleic acids is to know the sequence of at least part of the gene being targeted. The fact that the entire sequence of the apoE gene was available to Applicants would make it clear to those skilled in the art that Applicants had possession of a method involving reducing expression of apoE. Given the availability of apoE nucleotide sequences, the skilled artisan would also know the corresponding antisense, ribozyme, and antisense conjugate sequences. As it is well established that a "patent need not teach, and preferably omits, what is well known in the art," Applicants need not reiterate every antisense, ribozyme, and antisense conjugate sequence that falls within the scope of the claims. See MPEP §2164.01. Accordingly, Applicants contend that in light of the availability of apoE nucleotide sequences, the skilled artisan would recognize that the Applicants were in possession of the claimed invention.

Applicants submit that the rejection of claims 1, 4-8, and 11 under 35 U.S.C. §112, first paragraph, has been adequately addressed in view of the remarks set forth above. The Examiner is thus respectfully requested to withdraw the rejection.

Rejections under 35 U.S.C.§102(b)

Claims 1, 4-8, and 11 were rejected under 35 U.S.C.§102(b) as allegedly anticipated by Ditschuneit et al. ((1992) *J. Int'l. Med. Res.* 20:197-210; "Ditschuneit") as evidenced by Pedreño et al. ((2000) *Metabolism* 49:942-949; "Pedreño") and Durrington et al. ((1998) *Atherosclerosis* 138:217-225; "Durrington"). Claims 1, 4-8, and 11 were rejected under 35 U.S.C.§102(b) as allegedly anticipated by Yoshino et al. ((1989) *Atherosclerosis* 75:67-72; "Yoshino"). Claims 1, 4-8, and 11 were rejected under 35 U.S.C.§102(b) as allegedly anticipated by Connor et al ((1993) *Ann. N.Y. Acad. Sci.* 683:16-34; "Connor"). Claims 1, 5, 6, and 11 were rejected under 35 U.S.C.§102(b) as allegedly anticipated by Kasiskie et al. ((1990) *Am. J. Kidney Dis.* 15:8-15; "Kasiskie") as evidenced by Wyne et al. ((1989) *J. Biol. Chem.* 264:16530-16536; "Wyne").

Applicants respectfully traverse the rejections under 35 U.S.C.§102(b). Applicants' position on these rejections has been made of record. Nevertheless, and solely in the interest of expediting prosecution, claims 1 and 5 are amended to recite administering to the host an effective amount of an agent selected from the group consisting of antisense nucleic acids, ribozymes, and antisense conjugates.

Claims 1, 4-8, and 11; Ditschuneit

The Office Action asserts that Ditschuneit et al. teaches a method of treating patients with hyperlipoproteinaemia type IV with gemfibrozil. The Office Action further asserts that Pedreno et al. and Durrington et al., teach that gemfibrozil causes a reduction in levels of triglyceride, VLDL and apoE in a patient. The Office Action asserts that all the limitations of the claims are anticipated by the teachings of Ditschuneit. Applicants respectfully traverse the rejection.

It is basic patent law that in order to anticipate a claim, a reference must teach each and every element of the claim. A claim is anticipated only if each and every element as set forth in the claim is found in a single prior art reference.[1]

Ditschuneit discusses treating patients with gemfibrozil. Gemfibrozil is not an antisense nucleic acid, ribozyme, or antisense conjugate. Thus, because Ditschuneit does not teach each and every element of the claimed invention, Ditschuneit does not anticipate claims 1, 4-8, and 11.

[1] *Verdegaal Bros. v. Union Oil of California*, 2USPQ2d 1051, 1053 (Fed. Cir. 1987).

Claims 1, 4-8, and 11; Yoshino

The Office Action asserts that Yoshino teaches a method for treating patients diagnosed with a disease associated with elevated plasma levels of VLDL and triglycerides, by administering pravastatin to reduce the concentrations of apoE, VLDL, and triglycerides. The Office Action asserts that Yoshino anticipates claims 1, 4-8, and 11. Applicants respectfully traverse the rejection.

Yoshino discusses methods of treating patients with pravastatin. Pravastatin is not an antisense nucleic acid, ribozyme, or antisense conjugate. Thus, because Yoshino does not teach each and every element of the claimed invention, Yoshino cannot anticipate claims 1, 4-8, and 11.

Claims 1, 4-8, and 11; Connor

The Office Action asserts that Connor teaches a method for treating patients diagnosed with a disease associated with elevated plasma levels of VLDL and triglycerides by administering an effective amount of dietary n-3 fatty acids. The Office Action asserts that all of the limitations of the claims are anticipated by Connor. Applicants respectfully traverse.

Connor discusses methods of treating patients with dietary n-3 fatty acids. Dietary n-3 fatty acids are not antisense nucleic acids, ribozymes, or antisense conjugates. Thus, because Connor does not teach each and every element of the claimed invention, Connor cannot anticipate claims 1, 4-8, and 11.

Claims 1, 5, 6, and 11; Kasiskie

The Office Action asserts that Kasiskie teaches a method for treating patients diagnosed with a hyperlipidemia, involving administering an effective amount of lovastatin, an inhibitor of HMG-CoA reductase. The Office Action further asserts that the teachings of Wyne indicate that mevinolin (lovastatin) attenuates production of mRNA encoding apoE in cells. The Office Action asserts that all of the limitations of the claims are anticipated by Kasiskie. Applicants respectfully traverse.

Kasiskie discusses methods of treating patients with lovastatin (mevinolin). Lovastatin is not an antisense nucleic acid, ribozyme, or antisense conjugate. Thus, because Kasiskie does not teach each and every element of the claimed invention, Kasiskie cannot anticipate claims 1, 5, 6, and 11.

Conclusion as to the rejections under 35 U.S.C.§102(b)

Applicants submit that the rejections of claims 1, 4-8, and 11 under 35 U.S.C. §102(b) have been adequately addressed in view of the remarks set forth above. The Examiner is thus respectfully

requested to withdraw the rejections.

III. CONCLUSION

Applicants submit that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number UCAL121.

Respectfully submitted,
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Date: Aug. 1, 2005

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